

AMENDMENTS TO THE SPECIFICATION

At page 10, please delete the three paragraphs after the heading "Brief Specification of the Drawings" (beginning at line 17) and replace them with the following new paragraph:

Figures 1A - 1C show the base sequence (SEQ ID NO:2) of DNA encoding for the protein of the present invention obtained in Example 2, and the amino acid sequence which is encoded by it (SEQ ID NO:1).

At page 11, please amend the first paragraph (lines 1-3) as follows:

Figure [[4]] 2 shows a comparison of homologies on the amino acid sequences of ribonucleotide reductase and the protein of the present invention obtained in Example 2.

At page 11, please amend the second paragraph (lines 4-5) as follows:

Figure [[5]] 3 shows changes in the expressed amounts of R2 mRNA and TP53R2H mRNA after DNA damage obtained in Example 3.

At page 11, please amend the third paragraph (lines 6-8) as follows:

Figure [[6]] 4 shows DNA repair activity through ribonucleotide reductase activity during induction of expression of the TP53R2H obtained in Example 4.

At page 11, please amend the fourth paragraph (lines 9-11) as follows:

Figure [[7]] 5 shows DNA repair activity through ribonucleotide reductase activity when TP53R2H expression was suppressed by using the antisense oligonucleotide obtained in Example 5.

At page 11, please amend the fifth paragraph (lines 12-14) as follows:

Figure [[8]] 6 shows the short-term cell survival rate when TP53R2H activity was suppressed by using the antisense oligonucleotide obtained in Example 5, and the DNA damage was given.

At page 11, please amend the sixth paragraph (lines 15-16) as follows:

Figure [[9]] 7 shows the effect on DNA damage when the stable transformant of TP53R2H obtained in Example 6 was prepared and TP53R2H strongly expressed.

At page 83, please amend the paragraph beginning at line 13 as follows:

The sequences of the oligonucleotides AS3, SE3 and p53AS used in Example 5 below are shown here in that order.

AS3: A₅C₅A₅T₅T₅T₅A₅C₅C₅T₅C₅A₅T₅C₅C₅T (SEQ ID NO: 15)

SE3: A₅G₅G₅A₅T₅G₅A₅G₅G₅T₅A₅A₅A₅T₅G₅T (SEQ ID NO: 16)

p53AS: C₅C₅C₅T₅G₅C₅T₅C₅C₅C₅C₅C₅C₅T₅G₅G₅C₅T₅C₅C (SEQ ID NO: 17)

At page 85, please amend the paragraph beginning at line 6 and continuing to page 86, line 2, as follows:

An EST search was performed on the sequence obtained in Example 1, and Primers 1 and 2 were prepared based on the extended sequence. mRNA was extracted from the SW480WTP53 0, 8, 16, 24, 32 and 40 hours after addition of isopropyl β -D-thiogalactopyranoside, RT-PCR was performed using cDNA synthesized with oligo (dT) 12-18 primer as the template, an induction of TP53R2H expression was confirmed. Induction of expression of this cDNA fragment was also confirmed in Northern blot analysis (aforementioned m-RNA sample) using a probe prepared from the aforementioned PCR product, and the transcription product was confirmed to be about 5.5 kb in size. The same probe was used to screen a human skeletal muscle derived cDNA library (10^6 plaques), resulting in a 4368 bp cDNA fragment. The 5' end was extended by the 5' RACE method using a Marathon cDNA Amplification Kit (Clontech). The template for the extension reaction was cDNA prepared from human placenta mRNA (Clontech) using a Marathon cDNA Amplification Kit (Clontech). 1st PCR was performed using Primer 3 and Primer AP1 (part of the aforementioned Marathon cDNA Amplification Kit), and 2nd PCR using Primer 4 and Primer AP2 (part of the aforementioned Marathon cDNA Amplification Kit), resulting in a cDNA fragment with a base sequence of 4955 bp including 587 bp extension of the 5' end. A 1053 bp ORF (Open Reading Frame) encoding 351 amino acids was discovered in this 4955 bp cDNA sequence (~~Figures 1-3~~Figures 1A - 1C). A homology search of this amino acid sequence revealed that the amino acid sequence had about 80% homology with the small subunit (R2) of human-derived ribonucleotide reductase (Figure [[4]]_2).

At page 87, please amend the paragraph beginning at line 3 as follows:

The results showed almost no expression of TP53R2H in SW480 and H1299, with expression increasing over time only in NHDF and MCF7. Expression of R2 did not change in SW480 and H1299, but decreased over time in NHDF and MCF7 (Figure [[5]]_3).

At page 88, please amend the paragraph beginning at line 7 as follows:

In MCF7, the results confirmed an increase in DNA repair activity over time after DNA damage when induction of TP53R2H was confirmed in Example 3. When the same experiment was performed using H1299 which lacked normal p53 and in which TP53R2H expression was not induced, there was only a slight rise in DNA repair activity (Figure [[6]]_4).

At page 88, please amend the paragraph bridging pages 88-89 as follows:

The results confirmed that DNA repair activity declined when TP53R2H expression was suppressed with an antisense oligonucleotide (AS3). DNA repair activity also declined when p53 expression was suppressed with a p53 antisense oligonucleotide (p53AS) (Figure [[7]]_5).

At page 89, please amend the paragraph beginning at line 17 as follows:

The results confirmed that in both the short- and long-term, when TP53R2H expression is suppressed with an antisense oligonucleotide (AS3), sensitivity to DNA damage increases and cell death is more likely. Similar

results were observed using the p53 antisense oligonucleotide (p53AS) (Table 1 and Figure [[8]]_6).

At page 90, please amend the paragraph beginning at line 16 as follows:

The results confirmed that in H1299 which strongly express TP53R2H, sensitivity to DNA damage (adriamycin 0.2 μ g/ml) is reduced and cell death suppressed (G2/M arrest occurs) (Figure [[9]]_7).

At page 94, after the heading "Abstract", please amend the paragraph as follows:

~~Because the protein of the present invention has in its amino acid sequence a homology with, for example,~~ A protein having ribonucleotide reductase activity, the protein of the present invention, its DNA encoding the protein, antibodies to these and the like are disclosed. The protein, DNA and antibodies are useful in the prevention, treatment and diagnosis, etc. of cancer.